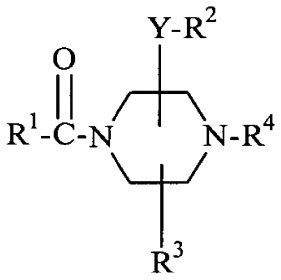
REMARKS

Applicants thank the Examiner and his supervisor for the courtesy extended to Applicants' attorney during the interview held August 9, 2000, in the above-identified application. During the interview, Applicants' attorney addressed the issues raised in the Office Action, especially the restriction requirement and the rejection under 35 U.S.C. §112, first paragraph. The discussion is summarized and expanded upon below.

The present invention is drawn to a piperazine compound of the formula:



wherein

Y is bond or lower alkylene,

R^1 is aryl which may have substituent(s),

R^2 is aryl or indolyl, each of which may have substituent(s),

R^3 is hydrogen or lower alkyl,

R^4 is selected from a particular Markush group as recited in Claim 1.

No prior art has been applied against the claimed invention.

The present invention is disclosed as having Tachykinin antagonism activity, and is thus useful for treating or preventing Tachykinin-mediated diseases.

Applicants' Assignee has filed patent applications and received U.S. patents on other piperazine derivatives having Tachykinin antagonism activity, and having a chemical

structure similar to that of the presently-claimed compound, but having a different group at the R^4 position. Such patents, as well as patent applications, have been identified in the Information Disclosure Statement (IDS) and List of Related Cases, filed March 7, 2000. Examples of such patents include U.S. 5,670,505 and U.S. 6,087,357, which issued from Serial No. 09/091,269. These references, as well as references cited in the International Search Report, show that the piperazine core of the presently-claimed compounds are old, and that compounds having such a core are known for the presently-disclosed utility regarding Tachykinin antagonism.

Prior to addressing both the Restriction Requirement, and the rejection under 35 U.S.C. §112, first paragraph, Applicants note that the Examiner's assertion, at paragraph 1 at page 4 of the Office Action, that the application does not contain an Abstract of the Disclosure, is incorrect. An Abstract on a separate sheet was submitted with the original application as page 194. **Submitted herewith** is another copy of this page.

The restriction requirement

The Office, citing PCT Rules 13.1 and 13.2, contends that the claims lack unity of invention because "they represent different cores and use."

The restriction and election requirements continue to be traversed. Applicants note that the PCT administrative instructions in the MPEP, Annex B, Part 1(f) define Markush practice and state that the alternatives defined in a single claim shall meet the technical relationship requirements of PCT Rule 13.2 if they are of a similar nature. These alternatives shall be regarded as being of a similar nature when the following criteria are fulfilled:

(A) all the alternatives have a common property or activity, and

(B)(1) a common structure is present, i.e., a significant structural element is shared by all of the alternatives, or

(B)(2) in cases where the common structure cannot be the unifying criteria, all alternatives belong to a recognized class of chemical compounds in the art to which the invention pertains.

The Office provides no support for its conclusion that the alternative chemical compounds in the claims are so dissimilar that they fail to meet the requirements of PCT Rule 13.2 for Markush practice. Applicants respectfully submit that each of criteria (A) and (B) is met by the compounds under the claims and that they are of similar nature as that term is defined in Annex B above. Accordingly, Applicants respectfully submit that the restriction and election requirements are improper and respectfully request that they be withdrawn.

Applicants respectfully traverse the restriction and election of species requirements on the additional ground that the Office has not shown that a burden exists in searching all of the claims. MPEP §803 states as follows:

> "If the search and examination of an entire application can be made without a serious burden, the Examiner must examine it on the merits, even though it includes claims to distinct or independent inventions."

Applicants respectfully submit that a search of all the claims would not impose a serious burden on the Office.

In the Office Action, the Examiner asserts that the search of the entire invention would be burdensome. However, Applicants respectfully submit that the Examiner already has the closest prior art. Moreover, given the computer capabilities existing today, the argument that the various groups are classified differently, while perhaps true, is not synonymous with added burden.

Office policy provides that even in cases where a restriction requirement is otherwise proper, if there is no undue burden, the entire application must be examined. However, Office policy is **not** that undue burden is sufficient for restriction purposes when the restriction requirement is not otherwise proper. Thus, even if there is undue burden, and Applicants do not agree that there is, the restriction requirement herein is improper, for reasons above stated.

The Examiner also asserts concepts related to U.S. restriction requirement practice. However, the present application is a national stage application under the PCT, and thus unity of invention requirements, not U.S. restriction requirements, apply.

The Examiner has concluded that there is lack of unity of invention by asserting that there is lack of unity of invention! But the Examiner has not shown, nor can the Examiner show, that Applicants do not meet the requirements of unity of invention, as discussed above.

As discussed at the above-referenced interview, Applicants respectfully submit that the restriction requirement is improper and should be withdrawn. If it is not withdrawn, then Applicants respectfully request that it be at least reformatted so as not to divide up particular heterocyclic moieties in the definition for R^4.

Applicants affirm the election of Group I, as required by the Examiner.

The rejection under 35 U.S.C. §112, first paragraph

The rejection of Claims 1-10 under 35 U.S.C. §112, first paragraph, as lacking sufficient enabling disclosure to make and/use the invention as claimed, is respectfully traversed. The Examiner asserts, *inter alia*, that "there's no reasonable basis for assuming that the myriad of compounds embraced by the generic claims will all share the same pharmacological/physiological properties", that "there is no relevant test/assay data

with/without inclusion of art recognized compounds proving the novelty and superior performance of the instantly claimed compounds", and that "the applicants do not provide comparative results/assays to support their claimed novel compounds' performance for human beings." The Examiner's assertions, however, are not based on present law.

A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. §112, first paragraph, unless there is a reason to doubt the objective truth of the statement contained therein which must be relied on for enabling support. The first paragraph of 35 U.S.C. §112 requires nothing more than objective enablement. See In re Marzocchi, 439 F2d 220, 169 USPQ 367 (CCPA 1971). See also In re Brana, 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995) and M.P.E.P. 2164.04. The Examiner has set forth no reasons why one skilled in the art would doubt the truth of any statement in Applicants' disclosure.

The above-discussed prior art provides convincing evidence that Tachykinin antagonism activity is not speculative and the close structural similarity (although not legally obvious) of prior art compounds, as well as the present disclosure, indicates that one skilled in the art would be enabled to make the claimed compounds. The present invention is clearly sufficiently enabled.

For all the above reasons, it is respectfully requested that the rejection under 35 U.S.C. §112, first paragraph, be withdrawn.

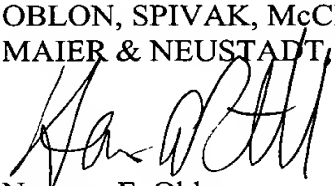
Prior art and related cases

Applicants note the Examiner's request at the last paragraph of page 8 of the Office Action with regard to related cases. In response, Applicants point out the IDS and related cases statement discussed above. In addition, the Examiner is reminded that according to the Notice published in 1156 Off. Gaz. Pat. Office 91 (November 23, 1993), and MPEP 609 (7th ed., Rev. 1, Feb. 2000, page 600-99), in PCT national stage applications, when the Form PCT/DO/EO/903 indicates that both the International Search Report and copies of the references cited therein have been received by PTO, the Examiner **will** consider the references and should state for the record that the references have been considered. In view of such form of date February 29, 2000 in this application, **Applicants respectfully solicit the Examiner to consider these references and to explicitly state that for the record.**

All of the presently pending claims in this application are now believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.



Norman F. Oblon
Attorney of Record
Registration No. 24,618

Harris A. Pitlick
Registration No. 38,779

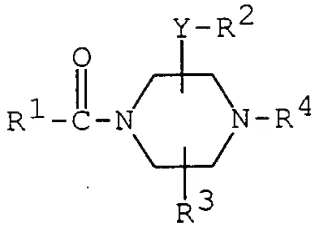
22850

(703) 413-3000
Fax #: (703) 413-2220
NFO/HAP:

I:\atty\HAP\00181086.am.wpd

A B S T R A C T

This invention relates to piperazine derivatives of the formula :



wherein each symbol is as defined in the description, and its pharmaceutically acceptable salt, to processes for preparation thereof, to pharmaceutical composition comprising the same, and to a use of the same for treating or preventing Tachykinin-mediated diseases in human being or animals.